REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
20 June 2011	**FINAL**	1 Jun 2009 - 30 Nov 2010

4. TITLE AND SUBTITLE

Efficacy of Silver Nanoparticle Gel on Bacterial Hand Flora: A RCT

5a. CONTRACT NUMBER
N/A

5b. GRANT NUMBER
HU0001-09-1-TS03

5c. PROGRAM ELEMENT NUMBER
N/A

6. AUTHOR(S)

Schlicher, Michael L., PhD, RN, COL, AN, USA

5d. PROJECT NUMBER
N09-002

5e. TASK NUMBER
N/A

5f. WORK UNIT NUMBER
N/A

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Henry M. Jackson Foundation
1401 Rockville Pike, Suite 600
Rockville, MD 20852

8. PERFORMING ORGANIZATION REPORT NUMBER
N/A

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

TriService Nursing Research Program, 4301 Jones Bridge RD
Bethesda, MD 20814

10. SPONSOR/MONITOR'S ACRONYM(S)
TSNRP

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
N09-002

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES
N/A

14. ABSTRACT

Purpose: The purpose of this study was to compare the antimicrobial efficacy of a silver nanoparticle gel versus an alcohol-based hand gel versus a combo gel in reducing transient bacterial counts isolated from hands seeded with S. marcescens. **Design:** A randomized-controlled, double-blinded, 3-group (alcohol-based gel vs. silver nanoparticle gel vs. combination gel) design. **Methods:** Qualified subjects began participating in a 7-day washout period prior to hand sampling. Participants were randomly assigned to one of two conditions: immediate or persistent. *Baseline bacterial samples were obtained from artificially seeded hands using a modified glove juice technique. For the immediate condition, sampling of the surrogate marker microbes was taken after 1 minute of the gel application using the same procedure as in the baseline sampling. Participants in the persistent condition received the assigned gel first. After 30 minutes, the participant's hands were inoculated with the transient marker.* Sampling was completed using the same glove juice procedure as before. After decontaminating subject's hands, a 4-item questionnaire on gel acceptability was completed. **Sample***:* Fifty-five individuals were recruited from the Fort Sam Houston, TX campus. **Analysis:** Analysis of variance (ANOVA) and/or other appropriate normality tests were used for data analysis. **Findings:** For the immediate efficacy, test revealed a statistical significant difference between the alcohol-based gel and the silver nanoparticle gel (p=0.009 – 0.003) and a trend towards significance between the alcohol-based hand gel and the combination gel. The analysis found no statistical significant difference (p=0.33) between the gels for persistent efficacy. User acceptability was more favorable for the alcohol-based gel group. **Implications Military Nursing:** This study addressed the efficacy of two novel gels on bacterial counts with the results potentially informing future clinical effectiveness studies aimed at improving deployment health and the health of injured soldiers.

15. SUBJECT TERMS

hospital-associated infection (HAI), nanotechnology. infectious disease, deployment health,

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			Debra Esty
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UU	25	**19b. TELEPHONE NUMBER** *(include area code)* 301-319-0596

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TriService Nursing Research Program Final Report Cover Page

Sponsoring Institution	TriService Nursing Research Program
Address of Sponsoring Institution	4301 Jones Bridge Road Bethesda MD 20814
USU Grant Number	HU0001-09-1-TS03
USU Project Number	N09-002
Title of Research Study or Evidence-Based Practice (EBP) Project	Efficacy of Silver Nanoparticle Gel on Bacterial Hand Flora: A RCT
Period of Award	1 June 2009 – 30 November 2010
Applicant Organization	Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc
Address of Applicant Organization	1401 Rockville Pike, Suite 600 Rockville, MD 20852

Principal Investigator (PI) Military Contact Information: LTC Michael L. Schlicher, PhD

Duty Title	
Address	
Telephone	
Mobile Telephone	
E-mail Address	

PI Home Contact In

Address	
Telephone	
Mobile Telephone	
E-mail Address	

Signatures

PI Signature

Table of Contents

Abstract

Purpose: The purpose of this study was to compare the antimicrobial efficacy of a silver nanoparticle gel versus an alcohol-based hand gel versus a combo gel in reducing transient bacterial counts isolated from hands seeded with *S. marcescens*.

Design: A randomized-controlled, double-blinded, 3-group (alcohol-based gel vs. silver nanoparticle gel vs. combination gel) design.

Methods: Qualified subjects began participating in a 7-day washout period prior to hand sampling. Participants were randomly assigned to one of two conditions: immediate or persistent. Baseline bacterial samples were obtained from artificially seeded hands using a modified glove juice technique. For the immediate condition, sampling of the surrogate marker microbes was taken after 1 minute of the gel application using the same procedure as in the baseline sampling. Participants in the persistent condition received the assigned gel first. After 30 minutes, the participant's hands were inoculated with the transient marker. Sampling was completed using the same glove juice procedure as before. After decontaminating subject's hands, a 4-item questionnaire on gel acceptability was completed.

Sample: Fifty-five individuals were recruited from the Fort Sam Houston, TX campus.

Analysis: Analysis of variance (ANOVA) and/or other appropriate normality tests were used for data analysis.

Findings: For the immediate efficacy, tests revealed a statistical significant difference between the alcohol-based gel and the silver nanoparticle gel ($p = 0.009 - 0.03$) and a trend towards significance between the alcohol-based hand gel and the combination gel. The analysis found no statistical significant difference ($p = 0.33$) between the gels for persistent efficacy. User acceptability was more favorable for the alcohol-based gel group.

Implications for Military Nursing: This study addressed the efficacy of two novel gels on bacterial counts with the results potentially informing future clinical effectiveness studies aimed at improving deployment health and the health of injured soldiers.

TSNRP Research Priorities that Study or Project Addresses

Primary Priority

Force Health Protection:	☐ Fit and ready force ☒ Deploy with and care for the warrior ☐ Care for all entrusted to our care
Nursing Competencies and Practice:	☐ Patient outcomes ☐ Quality and safety ☐ Translate research into practice/evidence-based practice ☐ Clinical excellence ☐ Knowledge management ☐ Education and training
Leadership, Ethics, and Mentoring:	☐ Health policy ☐ Recruitment and retention ☐ Preparing tomorrow's leaders ☐ Care of the caregiver
Other:	☐

Secondary Priority

Force Health Protection:	☐ Fit and ready force ☐ Deploy with and care for the warrior ☐ Care for all entrusted to our care
Nursing Competencies and Practice:	☐ Patient outcomes ☐ Quality and safety ☐ Translate research into practice/evidence-based practice ☐ Clinical excellence ☐ Knowledge management ☐ Education and training
Leadership, Ethics, and Mentoring:	☐ Health policy ☐ Recruitment and retention ☐ Preparing tomorrow's leaders ☐ Care of the caregiver
Other:	☒ Military clinical practice and outcomes management

Progress Towards Achievement of Specific Aims of the Study or Project

Findings related to each specific aim, research or study questions, and/or hypothesis:

Due to the non-normality of the data, the colony forming units (CFUs) data were log transformed prior to data analysis. Every effort was made to maintain equality of subject groups; however, distribution into equal groups ended up being unequal due to recruitment and retention issues.

- **Specific Aim #1**: Compare the immediate antimicrobial efficacy of three gels, a silver nanoparticle gel (SilvaSorb™, AcryMed, Inc., Portland, OR) versus an alcohol-based hand gel (Purell™, GoJo Industries, Akron, OH) versus a combo gel (mixture of both alcohol and silver gels) in reducing transient bacterial counts isolated from hands seeded with *S. marcescens.*

  Null hypothesis: There is no significant difference in the immediate antimicrobial efficacy between or within groups who received either a silver nanoparticle gel, an alcohol-based gel, or a combination gel one minute after application, as measured by a reduction of transient bacteria isolated from seeded hands.

  An ANOVA was performed which found a statistical significant difference ($p = 0.02$) between gel groups (Table 1). Tukey's, Bonferoni's, and Fisher's Least Significant Difference tests all revealed a statistical significant difference between the alcohol-based gel and the silver nanoparticle gel for the immediate effect. Furthermore, there was a trend towards significance between the alcohol-based hand gel and the combination gel since all of the p-values were less than 0.09.

Table 1: ANOVA results for immediate efficacy for the test gels.

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	34.211	2	17.105	4.457	.017
Within Groups	191.906	50	3.838		
Total	226.117	52			

- **Specific Aim # 2**: Compare the persistent antimicrobial efficacy of three gels, a silver nanoparticle gel versus an alcohol-based hand gel versus a combination gel at baseline and 30 minutes after gel application in reducing transient bacterial counts isolated from hands seeded with *S. marcescens.*

Null hypothesis: There is no significant difference in antimicrobial efficacy between or within groups who received either a silver nanoparticle gel, an alcohol-based gel, or a combination gel 30 minutes after application, as measured by a reduction of transient bacteria isolated from seeded hands.

An ANOVA was performed which found no statistical significant difference (p=0.33) between the groups (Table 2). Based on the results of this analysis, this study suggests that there is no advantage to using one gel over another for persistent efficacy.

Table 2: ANOVA results for persistent efficacy for the test gels.

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5.994	2	2.997	1.125	.333
Within Groups	133.200	50	2.664		
Total	139.194	52			

- **Specific Aim # 3**: Compare user acceptability of a silver nanoparticle gel versus an alcohol-based hand gel versus a combination gel using a self-assessment questionnaire.

Null hypothesis: There is no significant difference between acceptability ratings for a silver nanoparticle gel group compared to an alcohol-based hand gel group or a combo group.

Aim 3 compared user acceptability between the groups of subjects who received the silver nanoparticle gel versus the alcohol-based hand gel versus the combination gel. An ANOVA test was used to determine the subject's perception of acceptability differences between the three gels. Acceptability of the gels used in the study differed significantly across the three gels, F (2, 52) = 10.735, p = 0.000 (Table 3). Tukey post hoc comparisons of the three gels revealed that the alcohol-based hand gel (M = 33.7, 95% CI [30.5, 37]) had a statistically significant higher acceptability rating compared to the silver nanoparticle hand gel (M = 18.5, 95% CI [12.0, 25.1]), p = .00. The alcohol-based hand gel also demonstrated a statistically significant higher acceptability rating compared to the combination gel (M=25.7, 95% CI [20.0, 31.5]), p = 04. Comparisons between the silver nanoparticle gel and the combination gel were not statistically significant at $p < .05$. The modified acceptability questionnaire revealed that scores ranged from 6 to 40 (highest acceptability score possible) with a mean score of 27 (SD = 11.7) (Figure 1).

Table 3: ANOVA results for overall acceptability of test gels.

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	2147.648	2	1073.824	10.735	.000
Within Groups	5201.698	52	100.033		
Total	7349.345	54			

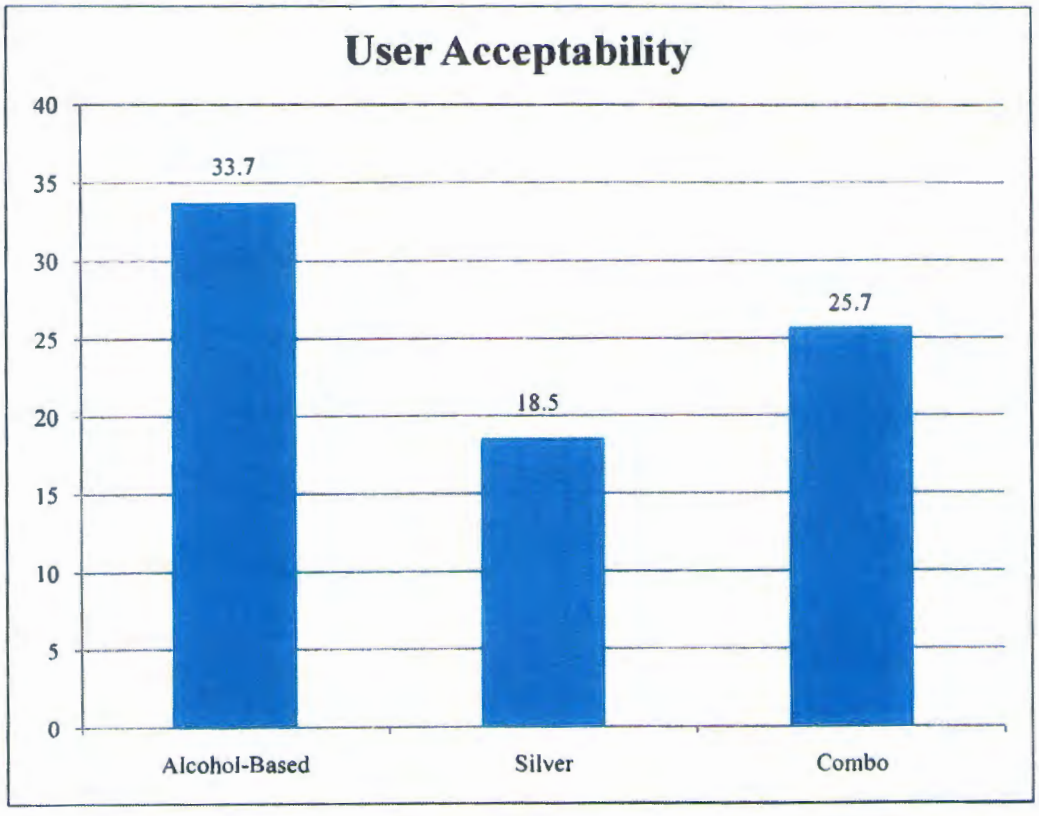

Figure 1: User acceptability of gel group. Range from 6 (lowest) to 40 (highest).

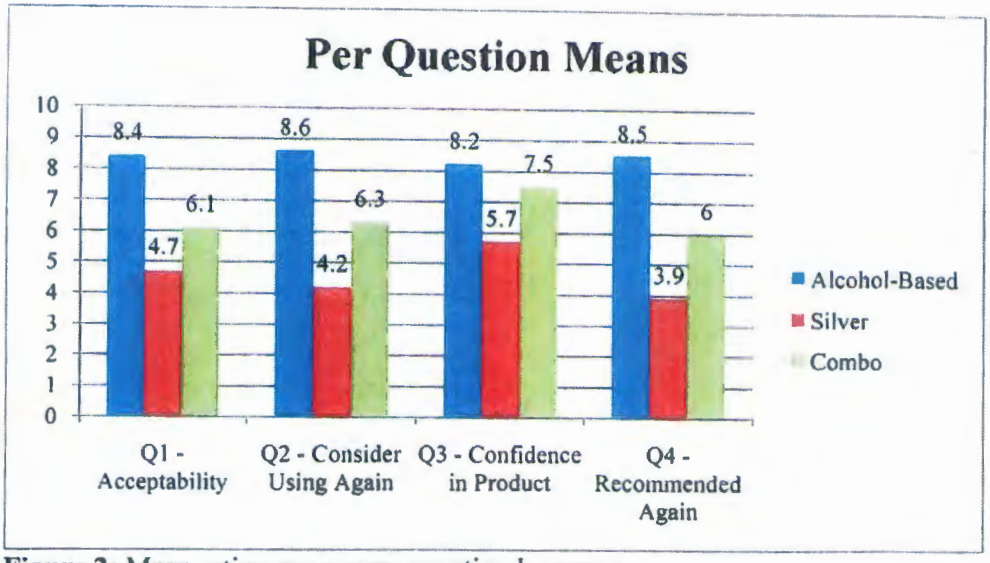

Figure 2: Mean rating per survey question by group.

Table 4: ANOVA results for acceptability of test gels per survey question.

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Acceptability Questionnaire - I would rate my acceptance of this product as? Really not acceptable to Really acceptable (1-10)	Between Groups	134.219	2	67.109	9.393	.000
	Within Groups	371.527	52	7.145		
	Total	505.745	54			
Acceptability Questionnaire - I would consider using this product again? Really would not consider using to Really would consider using (1-10)	Between Groups	176.528	2	88.264	11.486	.000
	Within Groups	399.582	52	7.684		
	Total	576.109	54			
Acceptability Questionnaire - I would rate my confidence in this product as? Lowest confidence to Highest confidence (1-10)	Between Groups	60.264	2	30.132	5.232	.009
	Within Groups	299.482	52	5.759		
	Total	359.745	54			
Acceptability Questionnaire - I would recommend using this product to my friends or co-workers? Definitely would not recommend to Definitely would recommend (1-10)	Between Groups	197.073	2	98.536	11.420	.000
	Within Groups	448.672	52	8.628		
	Total	645.745	54			

Mean ratings per question by group are depicted in Figure 2. ANOVA analysis by question revealed that there was a significant difference in the questionnaire responses between the three gels (Table 4). Question 1 explored the acceptance of the product. Of the three gels, post hoc analysis suggested that the alcohol-based hand gel was the best-accepted gel. The analysis demonstrated a statistical significant difference between the alcohol-based gel in comparison to the silver nanoparticle gel ($p = 0.00$) and the combination gel ($p = 0.20$). Gel usability (Question 2) also demonstrated a statistical significant difference between the alcohol-based hand gel and the silver nanoparticle gel ($p = 0.00$) and again between the alcohol-based hand gel and the combination gel ($p = 0.04$). Regarding confidence in the product (Question 3), the analysis only demonstrated a statistical significant difference between the alcohol-based hand gel and the silver nanoparticle gel ($p = 0.01$). There was not a statistical significant difference in confidence rating between the alcohol-based had gel and the combination gel ($p = 0.65$). When considering recommending the product (Question 4), both the silver nanoparticle gel and the combination gel were less likely to be recommended than the alcohol-based hand gel ($p = 0.00$ and $p = 0.03$, respectively).

Relationship of current findings to previous findings:

This study builds on a randomized controlled dissertation study of clinical research where the same silver nanoparticle gel used in this study was tested for its efficacy against the same alcohol-based gel as an alternative therapeutic to possibly decrease artificially seeded bacterial hand counts. The dissertation study used the same surrogate marker microbe, *S. marcescens*, and followed the same procedures to test for the immediate efficacy of the gels. In the dissertation study, persistent efficacy was tested after 10 minutes of gel application. This study expanded the length of time the gel was left on to 30 minutes to see if there was an improved reduction in CFU counts. Additionally, this study examined a new treatment arm using a 50/50 combination gel, whereas the original study used only the alcohol and silver arms.

The results of the dissertation study showed similar results as the study discussed here. For immediate efficacy, the alcohol-based gel produced a statistically significant difference in the log reduction of CFUs in comparison to the silver nanoparticle gel in the dissertation study as it did in this study. In the dissertation study, the silver nanoparticle gel produced a statistically significant difference in the log reduction of CFUs in comparison to the alcohol-based hand gel for persistent efficacy. However, with the present study, data did not support this finding. With regard to user acceptability, the dissertation study found that acceptability was more favorable for the alcohol-based gel group compared to the silver group but was not found to be statistically significant. The current study did reveal a statistically significant difference in the acceptability ratings between the alcohol-based gel and the silver nanoparticle gel. Participants rated the alcohol-based gel more favorable than the silver nanoparticle gel. No statistically significant difference was found between the other gels and the combination gel.

Findings from both studies are inconclusive and cannot influence recommendations of one gel over the other with respect to persistent efficacy. The complexity of testing procedures, laboratory conditions, additional treatment arms, increased times, and a small sample size may

have had direct consequences on the outcome of the present study. Additional studies are warranted to continue to test the validity and reliability of the testing procedures and to expand on the body of evidence supporting nanoparticle research.

Effect of problems or obstacles on the results:

As demonstrated in the recruitment and retention table on page 21, there were some retention problems with the proposed recruitment population. Over 95% of the individuals that volunteered at the first recruitment session failed to attend their scheduled testing appointment. The volunteers were new students in the Officer Basic Leadership Course and their schedule for the course was shortened by several days resulting in very limited free time. The research team provided the volunteers with a reminder postcard with their appointment information and contacted them via telephone or email a day prior to their testing appointment as an additional reminder of their participation in the study. Transportation to the hospital was an issue for many of the students, as they did not have a car available. As a solution to this retention issue, participation for this study was opened to other individuals on the Fort Sam campus. This change helped to recruit additional volunteers and proved to be extremely beneficial in increasing the compliance of the 7-day washout period. Although the research team expanded the recruitment population, this issue had a direct impact on the recruitment numbers and thus the research team was unable to meet the proposed number of participants in the study. Furthermore, this issue directly influenced the number of individuals in each testing group since the randomized list of testing conditions had been created prior to recruitment.

Additionally, Base Realignment and Closure (BRAC) requirements at Brooke Army Medical Center significantly influenced the availability of laboratory and testing space. During the height of recruitment, we were required to move from our established testing area several times and relocate to different parts of the building in order to accommodate BRAC renovations. Reliability of the laboratory equipment was also an issue. The study team encountered multiple problems throughout the study period with the autoclave and the lab incubators. The equipment was in a state of "being fixed" during most of the study period.

Limitations:

One of the limitations of this study was the lack of generalizability in regard to types of gels used, number of gel applications, type of bacteria, and populations. For instance, this study evaluated only one type of alcohol-based gel and one formula of silver nanoparticle gel. Gel products may vary in their formulation and perhaps other gels may or may not have produced the same results. Hence, testing of multiple gels in comparison to the control gel would be beneficial. Furthermore, although precautionary measures were taken to ensure that the combination hand gel consisted of 50% alcohol-based gel and 50% silver nanoparticle gel, a new batch of combination hand gel was created for each testing day and thus might have affected the overall results of this testing group. Equally important with the lack of generalizability was the limited number of gel applications for each of the test conditions. For both the immediate and persistent efficacy conditions, subjects were tested after only two applications of gel per condition. Double application is not consistent with current hand hygiene efficacy methodologies, which normally require up to 10 consecutive hand dosing and washing cycles [1]. Hence, any conclusions from this study must be considered as preliminary findings.

Another aspect of a two-time dosing regime is that even if a hand hygiene product is effective in removing transient bacteria and preventing re-growth, it must also be mild enough to the skin after several consecutive applications to avoid irritation and skin breakdown. If not, health care workers (HCWs) are unlikely to comply with handwashing protocols. Since test gels were only applied four times over the course of the testing, skin condition was not examined. However, future studies could include multiple applications of the gel to determine the effect on the condition of the skin. Skin condition after using consecutive applications of alcohol-based gels have been well established; [2-5] however, there have been no published studies that have examined the consecutive use of silver nanoparticle gel as a hand hygiene product and whether multiple applications cause irritation of the hands. Further investigation of this characteristic is reasonable and might include a longitudinal study where hands are examined before the start of therapy and again after several days of continued use.

A further limitation was that this study evaluated hand hygiene efficacy by utilizing a singular gram-negative bacterium. Ideally, hand hygiene products should be capable of broad-spectrum antimicrobial activity. The cell wall of a gram-negative bacterium, such as *S. marcescens*, differs significantly from that of a gram-positive bacterium. Because the gram-negative cell wall contain lipids, proteins, and lipopolysaccharides that theoretically provide protection against potential biocides, it is possible that the effects of nanosilver gel will be different with gram-positive bacterium. Alcohol gels have been well tested for both gram negative and gram-positive bacteria making the use of alcohol gels clinically useful. Although the utilization of additional bacteria in this study may have been more clinically relevant, it was not possible to safely introduce more than one bacterium to the subjects without potentially increasing the level of risk to both the subjects and the surrounding population. Nevertheless, investigation of the broad-spectrum antimicrobial activity of silver nanoparticle gel in a controlled laboratory environment would be a useful additional next study.

Another potential limitation is the American Society for Testing and Materials protocol of artificially seeding subjects' hands. Although this procedure is considered an acceptable testing standard, it is nonetheless an artificial system performed in a controlled environment. The relevance of artificially contaminating subjects' hands with a surrogate bacterium in place of actual clinical practice is not completely understood. Thus, more realistic field studies are needed to determine the reduction of actual bacterial counts on the hands of HCWs in relation to where they practice and how they actually wash their hands.

Studies have also shown that the antimicrobial efficacy of hand sanitizers is different among a given population of individuals [6-8]. As this study was limited to only young healthy adults, generalization to at-risk populations remains to be determined. The homogeneous sample for the study was drawn from a population at a military facility where the subjects did not have patient contact and where testing was conducted in a controlled environment, thus limiting more realistic field conditions. It might be possible to increase generalizability by designing a study where the same investigator performs the same reference procedures in a cross-over design study using the same sample.

In certain clinical settings, such as an intensive care unit, HCWs might experience greater than 30 handwashing opportunities per hour [9]. As this was an efficacy study, it was not possible to mimic more realistic field conditions where the hands of HCWs could be subjected to multiple episodes of handwashing in a relatively short period of time. Not performing multiple handwashing episodes limits the ability to directly compare outcomes with other studies. A possible next-step study might be to determine the effectiveness of silver nanoparticle gel for its

persistent antimicrobial activity by having the subject perform multiple hand hygiene episodes using the silver nanoparticle gel with each episode over several continuous hours. As a consequence of designing a more realistic field study, the effectiveness design might increase the external validity of the study (extent to which findings represent the true effect in a target population), and thereby build on the internal validity presently maximized by the current efficacy study.

The survey used in this study also warrants discussion as a limitation. As with any survey, there is a possibility of selection bias that might have impacted survey results either by under or over representing the population. For example, in this study subjects were selected from a target population that was not necessarily generalizable and therefore, may misrepresent the true population. In addition, response bias from problems with the survey measurement process cannot be ruled out. It is possible that some of the wording of the questions may have been framed to favor one response over another. Additionally, as most people like to present themselves in a favorable light, reluctance to admit unacceptable attitudes is common and could have resulted in bias toward responses subjects believed as socially desirable. The original acceptability survey developed by Larson and colleagues [10, 11] contained over 40 questions relating to user acceptability issues. The survey used in this study contained only four questions. As a result, a true representation of user acceptability cannot be confirmed by this study. Therefore, future studies might include the use of a survey that closely parallels previous acceptability surveys to allow for a better comparison of results.

Compliance of the washout period may also be a limitation of this study even though precautions were made to increase adherence of the washout period. All subjects were provided with a personal hand hygiene kit and asked to avoid using antibacterial soaps, shampoos, tanning lights, and harsh chemicals for a 7-day period prior to testing. A washout checklist was also developed to verify and establish accountability of subjects' compliance prior to testing. Based on questions from the checklist, 100% of the subjects reported they had complied with the washout stipulations. Nevertheless, verification was self-reported, subjective, and may have over-estimated actual adherence. Hence, there was no way to ensure that subjects complied with all avoidance instructions during the 7-day washout period. Although previous studies evaluating the efficacy of hand hygiene products made mention of the washout period, most did not indicate how compliance was established or verified.

Blinding of gel products might have been another possible limitation. Alcohol-based gels have a distinctive smell and could have easily been identified by subjects though all three gel products were unmarked, contained the same volume, and were distributed from the same type of container. Future hand hygiene studies, which require blinding, should ensure that gels are of the same consistency and smell to avoid any potential bias.

Another possible limitation was that this study did not compare the test gels with another known standard of hand hygiene, such as plain soap. According to the guidelines established by the Food and Drug Administration, with the exception of non-medicated soaps, every new formulation for hand antisepsis should be tested for its antimicrobial efficacy to demonstrate that: (i) it has superior efficacy over plain soap; and (ii) it meets safety standards [12]. This study did not compare the test gels to plain soap, so additional antimicrobial efficacy compared to alcohol gel could not be determined. Hence, the inclusion of normal soap group in future efficacy studies would be useful. Safety requires that the selected hand product produce no adverse reactions or any long term consequences that could be damaging to the patients [12].

This study did not evaluate any safety aspects of the test gels and as a result, may have limited the usefulness of the study in terms of efficacy.

A delay in plating may have been another possible limitation. Although plating was anticipated to be completed within 2 hours of sample collection, it was not physically possible given the limitations of personnel, time, and other logistical issues; however, specimens were plated within 8 hours of sampling. Previous studies by Larson [13, 14] showed that there was no significant increase or decrease in CFUs obtained from the solution if used within the first 2 hours after sampling. Hence, there can be no certanty as to the validity of the solution given that plating often exceeded more than 2 hours.

Finally, a problem referred to in the literature is the lack of studies evaluating hand hygiene products in order to determine whether they reduce healthcare-associated infections (HAIs). This study only compared the antimicrobial efficacies of three different hand gel formulations under controlled test conditions and was not designed to assess the effects of hand hygiene using the three gel products on HAIs. Although questionable due to the lack of immediate efficacy produced by the silver nanoparticle and the combo gel, a future study might include a sequential crossover design using two or more different hospital units to examine the impact of several hand hygiene products on CFU counts and reported unit HAIs. A sequential crossover design would help to minimize between-subject variability.

Conclusion:

The results of this randomized-controlled, double-blinded, demonstrated that the alcohol-based hand gel had a statistical significant immediate efficacy on bacterial counts in comparison to the silver nanoparticle gel and the combination gel. The study did not demonstrate immediate or persistent efficacy with the silver nanoparticle gel or the combination gel against bacterial counts. In addition, user acceptability favored the alcohol-based hand gel compared to the silver nanoparticle and combo gel. Because the results of this study differ from results of other studies, future research involving persistent efficacy is recommended. For example, because of the complexity of study procedures, validation is still a necessity. Additionally, newer silver nanoparticle hand gels are now available and could potentially influence the outcome. Lastly, evidence is lacking, yet needed, for alternative hand hygiene therapies that may decrease infection and microbial resistance in theater. Additional research is warranted to explore the antimicrobial benefits of using silver nanoparticle gel in a real-life field environment.

Significance of Study or Project Results to Military Nursing

This study aimed to address the efficacy of silver nano therapy on bacterial counts with the results potentially informing future clinical effectiveness studies aimed at improving deployment health. HAIs are an important source of serious morbidity and mortality for all patients, especially for the critically ill [15-18]. The impact of military field operations on HAIs has not yet been fully elucidated; although the incidence of war related infections [19-21] has increased significantly, making infection control a fundamental concern for all military healthcare providers. Studies have implicated the hands of healthcare workers and the increasing resistance of microbes to antibiotics as two principal factors for this increase [22]. Hand hygiene is an effective tool available to break the chain of infection, decrease HAI's, and improve patient safety. Deployed military healthcare providers are often unable to maintain proper hand hygiene due to limited access to water, soap, or cleansing agents. Although alcohol-based hand gels are available and their effectiveness in reducing most pathogens has been well established, limitations remain such as lack of persistent antimicrobial protection and potential skin irritation. Evidence is lacking, yet needed, for alternative hand hygiene therapies that may decrease infection and microbial resistance. Nanoparticles, particles smaller than 100nm, have emerged as a new class of therapeutics responsible for enhancing efficacy of various drugs and other products, while simultaneously decreasing side effects owing to the unique properties of the nano sized particles. Silver is one example of an important nanoparticle that is currently being tested for its unique antimicrobial properties. This study provided the research team with a unique opportunity to increase knowledge and participation in novel infection control therapies augmented through studying the effects of nanoscience technology on clinical nursing interventions and outcomes. New non-pharmacological agents must be investigated to provide alternative options for infection control therapies. Hence, this study aimed to compare the antimicrobial efficacy and user acceptance of a silver nanoparticle and a combination gel against a commercialized alcohol-based hand gel in producing an immediate and persistent decrease in transient bacteria on the seeded hands of healthy adult volunteers. Although inconclusive, the results of this study may help to build a foundation of evidence for future studies regarding the potential use of silver nanoparticle gel as a non-pharmaceutical antibacterial therapy. In addition, this study may serve as a model for related nursing investigations building on nanoscience and may contribute knowledge for military healthcare providers regarding infection control and prevention.

Changes in Clinical Practice, Leadership, Management, Education, Policy, and/or Military Doctrine that Resulted from Study or Project

None to date

References Cited

1. Donaldson, L.J. and M.G. Fletcher, *The WHO World Alliance for Patient Safety: towards the years of living less dangerously.* Med J Aust, 2006. **184**(10 Suppl): p. S69-72.
2. Houben, E., K. De Paepe, and V. Rogiers, *Skin condition associated with intensive use of alcoholic gels for hand disinfection: a combination of biophysical and sensorial data.* Contact Dermatitis, 2006. **54**(5): p. 261-7.
3. Larson, E., et al., *Assessment of two hand hygiene regimens for intensive care unit personnel.* Crit Care Med, 2001. **29**(5): p. 944-51.
4. Kampf, G. and A. Kramer, *Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs.* Clin Microbiol Rev, 2004. **17**(4): p. 863-93, table of contents.
5. Seal, L.A., R.L. Rizer, and R. Maas-Irslinger, *A unique water optional health care personnel handwash provides antimicrobial persistence and residual effects while decreasing the need for additional products.* Am J Infect Control, 2005. **33**(4): p. 207-16.
6. *World Health Organization. Prevention of Hospital-Acquired Infections: A Practical Guide*, in *World Health Organization*. 2002, WHO Press: Geneva.
7. Larson, E., *Effects of handwashing agent, handwashing frequency, and clinical area on hand flora.* Am J Infect Control, 1984. **12**(2): p. 76-82.
8. Rotter, M., ed. *Hand washing and hand disinfection.* 2nd ed. ed. Hospital epidemiology and infection contrtol, 2nd ed., ed. C.G. Mayhall. 1999, Lippincott Williams & Wilkins: Philadelphia.
9. Boyce, J.M. and D. Pittet, *Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America.* MMWR Recomm Rep, 2002. **51**(RR-16): p. 1-45, quiz CE1-4.
10. Larson, E., et al., *Physiologic and microbiologic changes in skin related to frequent handwashing.* Infect Control, 1986. 7(2): p. 59-63.
11. Larson, E., et al., *Prevalence and correlates of skin damage on the hands of nurses.* Heart Lung, 1997. **26**(5): p. 404-12.
12. FDA, *Topical antimicrobial drug products for over the counter human use: tentative final monograph for health-care antiseptic drug products.* Federal Register, 1994. **59**(116): p. 31402-31452.
13. Larson, E., P. Eke, and B. Laughon, *Efficacy of alcohol-based hand rinses under frequent-use conditions.* Antimicrob Agents Chemother, 1986. **30**(4): p. 542-4.
14. Larson, E., M. Strom, and C. Evans, *Analysis of three variables in sampling solutions used to assay bacteria of hands: type of solution, use of antiseptic neutralizers, and solution temperature.* J Clin Microbiol, 1980. **12**(3): p. 355-60.
15. Bearman, G.M., et al., *Infection control and the prevention of nosocomial infections in the intensive care unit.* Semin Respir Crit Care Med, 2006. **27**(3): p. 310-24.
16. Evans, H.L., et al., *Cost of Gram-negative resistance.* Crit Care Med, 2007. **35**(1): p. 89-95.
17. Stone, P.W., D. Braccia, and E. Larson, *Systematic review of economic analyses of health care-associated infections.* Am J Infect Control, 2005. **33**(9): p. 501-9.

18. Cosgrove, S.E., *The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs.* Clin Infect Dis, 2006. **42 Suppl 2**: p. S82-9.
19. Aronson, N.E., J.W. Sanders, and K.A. Moran, *In harm's way: infections in deployed American military forces.* Clin Infect Dis, 2006. **43**(8): p. 1045-51.
20. Murray, C.K., et al., *Bacteriology of war wounds at the time of injury.* Mil Med, 2006. **171**(9): p. 826-9.
21. Zapor, M.J. and K.A. Moran, *Infectious diseases during wartime.* Curr Opin Infect Dis, 2005. **18**(5): p. 395-9.
22. Boyce, J.M. and D. Pittet, *Guideline for Hand Hygiene in Health-Care Settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force.* Infect Control Hosp Epidemiol, 2002. **23**(12 Suppl): p. S3-40.

Summary of Dissemination

Type of Dissemination	Citation	Date and Source of Approval for Public Release
Publications	None to date	
Publications in Press	None to date	
Published Abstracts	None to date	
Podium Presentations	None to date	
Poster Presentations	Schlicher, M., McCarthy, M., Bingham, M., and Camou, E. "Efficacy of a Novel Silver Nanoparticle Gel Against Bacterial Hand Flora: A Randomized Controlled Trial" presented at the Phyllis J. Verhonick Nursing Research Course in San Antonio, TX on 26 April 2010.	03/2010 BAMC PAO/OPSEC
	Association of Military Surgeons of the United States 117th Annual Meeting in San Antonio, TX on 6-9 November 2011	Pending submission and approval.
Media Reports	None to date	

Other		

Reportable Outcomes

Reportable Outcome	Detailed Description
Applied for Patent	None
Issued a Patent	None
Developed a cell line	None
Developed a tissue or serum repository	None
Developed a data registry	None

Recruitment and Retention Table

Recruitment and Retention Aspect	Number		
Subjects Projected in Grant Application	90		
Subjects Available	90		
Subjects Contacted or Reached by Approved Recruitment Method	90		
Subjects Screened	90		
Subjects Ineligible	0		
Subjects Refused	0		
Human Subjects Consented	55		
Subjects Intervention Group 1 (Alcohol) / Intervention Group 2 (Silver)/ Intervention Group 3 (Combo)	30	30	30
Intervention Group 1 (Alcohol) / Intervention Group 2 (Silver)/ Intervention Group 3 (Combo) Subjects Who Withdrew	7	15	13
Intervention Group 1 (Alcohol) / Intervention Group 2 (Silver)/ Intervention Group 3 (Combo) Subjects Who Completed Study	23	15	17
Intervention Group 1 (Alcohol) / Intervention Group 2 (Silver)/ Intervention Group 3 (Combo) Subjects With Complete Data	22	15	16
Intervention Group 1 (Alcohol) / Intervention Group 2 (Silver)/ Intervention Group 3 (Combo) Subjects With Incomplete Data	1	0	1

Demographic Characteristics of the Sample

Characteristic	
Age (yrs)	28.4 ± 6.9
Women,	18 (32.7%)
Race	
White,	7 (38.9%)
Black,	5 (27.8%)
Hispanic or Latino,	3 (16.7%)
Native Hawaiian or other Pacific Islander,	0 (0%)
Asian,	1 (5.6%)
Other,	2 (11.1%)

Characteristic	
Age (yrs)	28.9 ± 6.1
Male,	37 (67.3%)
Race	
White,	24 (64.9%)
Black,	3 (8.1%)
Hispanic or Latino,	7 (18.9%)
Native Hawaiian or other Pacific Islander,	0 (0%)
Asian,	2 (5.4%)
Other,	1 (5.6%)

Final Budget Report

As seen in Appendix A, funds remaining totaled $11,696.18. The remaining funds can be attributed to the fact that the sample size was smaller than projected and that the laboratory provided the research team with more equipment than expected. Furthermore, the majority of the remaining funds are due to the fact that the PI and the AI were unable to expend the travel budget due to work- related commitments, thus leading to the inability to disseminate the results.

Please note, per Financial Department at the Henry M. Jackson Foundation, there are few outstanding vouchers still due on this award. DFAS was experiencing a delay in authorizing payment on submitted invoices. A revised Task Budget Summary will be submitted after the final payment is made.